REMARKS

At the outset, Applicants thank Examiner Roberts and her supervisor for their time and consideration of the above-identified application during the interview with the undersigned.

The issues raised in the outstanding Official Action of January 21, 2009, were discussed during the interview. The undersigned argued that the proposed combination of SIEBERT et al. in view of JARADAT et al. and MESTRE et al. fails to render obvious the claimed method of screening a selective inhibitor of COX-2.

The Examiner and Examiner's supervisor responded by stating that they were inclined to maintain the rejection. In doing so, it was explained that claim 6 was being construed in a manner that did not give full patentable weight to the preamble of the claim. In this regard, the Examiner and Examiner's supervisor indicated that it was not necessary to provide a combination of references directed to screening a selective inhibitor of COX-2.

The interview concluded without an agreement being reached as to any of the claims.

Claims 6 and 10 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over SIEBERT et al. in view of JARADAT et al. and MESTRE et al. This rejection is traversed.

SIEBERT et al. discloses a method for treating or preventing a neoplasia that produces prostaglandin in a subject in need of such treatment or prevention.

The method comprises treating the subject with a therapeutically effective amount of a COX-2 inhibitor or derivative thereof (col. 2, lines 10-15). SIEBERT et al. explains at col. 1, lines 15-42 that the administration of compounds that selectively inhibit COX-2 is preferable to administering NSAID compounds because the use of high doses of NSAIDS can produce severe side effects.

In imposing the rejection, the Official Action acknowledges that SIEBERT et al. fails to disclose a method for screening a selective inhibitor of COX-2 for the likelihood of success in treating a patient having or at risk for cancer, alzhemer's disease or atherosclerosis. In an effort to remedy the deficiencies of SIEBERT et al. for reference purposes, the Official Action cites to JARADAT et al. JARADAT et al. relates to the activation of peroxisome proliferator-activated receptor (PPAR) isoforms an inhibition of prostaglandin H_2 synthases by ibuprofen, naproxen, and indomethacin.

However, Applicants respectfully submit that the JARADAT et al. publication teaches away from SIEBERT et al. Ibuprofen, naproxen, and indomethacin are NSAIDS and not selective COX-2 inhibitors. As noted above, SIEBERT et al. teaches that the administration of NSAIDs can produce severe side effects. In this regard, one skilled in the art would have been dissuaded from combining the teachings of SIEBERT et al. with JARADAT et al.

The Examiner's attention is also directed to the two abstracts of articles from Nature Medicine attached to this Amendment. Contrary to the assertions of the Official Action, it would not have been obvious to test COX-2 inhibitors of SIEBART et al by screening for PPAR activation to help determine whether the

inhibitor would be successful in treating the neoplasia. The abstracts indicate that in some instances PPAR activation was actually linked to the development of tumors. In view of the information available to one skilled in the art at the time the application was filed, one skilled in the art would have plainly lacked the motivation to combine and modify SIEBERT et al. and JARADAT et al. in a manner that would result in the claimed invention.

The Official Action cites to MESTRE et al., wherein the inventor of the present application is a co-author, in a further effort to remedy the deficiencies of the rejection for reference purposes. MESTRE studies the inhibition of COX-2 as an approach to preventing head and neck cancers. In particular, MESTRE test for the suppression of EGFR mediated production of COX-2 with retinoids. However, MESTRE does not teach that selective COX-2 inhibitors exhibit this function. However, MESTRE et al. does not disclose or suggest cancer screening for certain properties of selective inhibitors of COX-2 as recited in the claims. In this regard, Applicants respectfully submit that MESTRE et al. fails to remedy the deficiencies of SIEBERT et al. and JARADAT et al. for reference purposes.

In view of the above, Applicants respectfully submit that one skilled in the art would lack the motivation to combine and modify the publications in a manner that would result in the claimed invention.

Nevertheless, even if one skilled in art were to combine the publications, one skilled in the art would still not have obtained the claimed invention. There is no recognition in any of the publications of a method for screening a selective

inhibitor of COX-2 for likelihood of success in treating a patient having or at risk for cancer, alzheimer's disease or atherosclerosis by testing for at least 2 of (a)-(g) as recited in claim 6. In this regard, Applicants most respectfully note that the last few lines of claim 6 recite that "the more of a, b, c, d, e, f and g being met, the greater the likelihood of success". This recitation plainly refers back to the preamble of the claim.

As the Examiner is aware, the determination of whether a preamble limits a claim is made on a case-by-case basis in light of the facts in each case; there is no litmus test defining when a preamble limits the scope of a claim. *Catalina Mktg. Int'l v. Coolsavings.com, Inc.*, 289 F.3d 801, 808, 62 USPQ2d 1781, 1785 (Fed. Cir. 2002). "If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is 'necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim." *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999). See also *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333, 68 USPQ2d 1154, 1158 (Fed. Cir. 2003).

As the preamble contains recitations present in the body of the claim that must be considered and the combination of publications fails to disclose or suggest a method for screening a selective inhibitor of COX-2 as noted above, Applicants respectfully request that the rejection be withdrawn.

In view of the present Amendment and foregoing Remarks, therefore, Applicants believe that the present application is in condition for allowance at the time of the next Official Action. Allowance and passage to issuance on that basis is respectfully requested.

Respectfully submitted,

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1: Nat Med. 1998 Sep;4(9):1053-7.

Activation of the peroxisome proliferator-activated receptor gamma promotes the development of colon tumors in C57BL/6J-APCMin/+ mice.

Lefebvre AM, Chen I, Desreumaux P, Najib J, Fruchart JC, Geboes K, Briggs M, Heyman R, Auwerx J.

LBRE, U.325 INSERM, Département d'Athérosclérose, Institut Pasteur, Lille, France.

The development of colorectal cancer, one of the most frequent cancers, is influenced by prostaglandins and fatty acids. Decreased prostaglandin production, seen in mice with mutations in the cyclooxygenase 2 gene or in animals and humans treated with cyclooxygenase inhibitors, prevents or attenuates colon cancer development. There is also a strong correlation between the intake of fatty acids from animal origin and colon cancer. Therefore, the peroxisome proliferator-activated receptor gamma (PPARgamma), a downstream transcriptional mediator for prostaglandins and fatty acids which is highly expressed in the colon may be involved in this process. Activation of PPARgamma by two different synthetic agonists increased the frequency and size of colon tumors in C57BL/6J-APCMin/+ mice, an animal model susceptible to intestinal neoplasia. Tumor frequency was only increased in the colon, and did not change in the small intestine, coinciding with the colon-restricted expression of PPARgamma. Treatment with PPARgamma agonists increased beta-catenin levels both in the colon of C57BL/61-APCMin/+ mice and in HT-29 colon carcinoma cells. Genetic abnormalities in the Wnt/wingless/APC pathway, which enhance the transcriptional activity of the beta-catenin-T-cell factor/lymphoid enhancer factor 1 transcription complex, often underly the development of colon tumors. Our data indicate that PPARgamma activation [illegible] the development of colon tumors in C57BL/61-

1: Nat Med. 1998 Sep;4(9):1058-61.

Activators of the nuclear receptor PPARgamma enhance colon polyp formation.

Saez E, Tontonoz P, Nelson MC, Alvarez JG, Ming UT, Baird SM, Thomazy VA, Evans RM.

The Salk Institute for Biological Studies, Howard Hughes Medical Institute, La Jolla, California 92037, USA.

A high-fat diet increases the risk of colon, breast and prostate cancer. The molecular mechanism by which dietary lipids promote tumorigenesis is unknown. Their effects may be mediated at least in part by the peroxisome proliferator-activated receptors (PPARs). These ligand-activated nuclear receptors modulate gene expression in response to fatty acids, lipid-derived metabolites and antidiabetic drugs. To explore the role of the PPARs in diet-induced carcinogenesis, we treated mice predisposed to intestinal neoplasia with a synthetic PPARgamma ligand. Reflecting the pattern of expression of PPARgamma in the gastrointestinal tract, treated mice developed a considerably greater number of polyps in the colon but not in the small intestine, indicating that PPARgamma activation may provide a molecular link between a high-fat diet and increased risk of colorectal cancer.

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